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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/575,377	05/22/2000	James J. Hickman	215177-00101	2330

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EXAMINER

ALLEN, MARIANNE P

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/575,377	HICKMAN, JAMES J.	
	<b>Examiner</b> Marianne P. Allen	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### **Status**

- 1) Responsive to communication(s) filed on \_\_\_\_\_.
- 2a) This action is **FINAL**.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### **Disposition of Claims**

- 4) Claim(s) 1-27 and 50 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-27 and 50 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### **Application Papers**

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### **Priority under 35 U.S.C. § 119**

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### **Attachment(s)**

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.	6) <input type="checkbox"/> Other: _____.

**DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 4/2/03 (after final amendment) and 6/3/03 have been entered.

Claims 28-49 have been cancelled. Claims 1, 15, 17, 20, 22-24, 27, and 50 have been amended. Claims 1-27 and 50 are under consideration by the examiner.

Applicant is requested to submit a complete listing of all claims in the application in compliance with the July 2003 revision of 37 CFR 1.121 in response to this Office action.

The rejection of claims 1-8, 12-14, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Jung et al. (*Journal of Vacuum Science & Technology*, 16(3):1182-1188, 1998) is withdrawn in view of the amendments to the claims and submission of the Hickman Declaration under 37 CFR 1.132. The Hickman Declaration asserts that the sensor disclosed in Jung et al. is not the same as that being claimed.

The rejection of claims 1-14, 18-19, and 23-27 under 35 U.S.C. 103(a) as being unpatentable over Borkholder et al. (U.S. Patent No. 6,377,057) in view of Jung et al. is withdrawn in view of the amendments to the claims and submission of the Hickman Declaration under 37 CFR 1.132.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Oath/Declaration***

Submission of the supplemental oath with the correct provisional application information is noted.

***Claim Rejections - 35 USC § 112***

Claims 1-27 and 50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a system having a microelectrode as set forth below, does not reasonably provide enablement for all intervening layers encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is an enablement rejection.

The claimed microelectrodes are required to have “an intervening layer in contact with the microelectrode surface, which (i) comprises a surface modifying agent, and (ii) is positioned between said microelectrode and the one or more cells of said cell culture, that provides a high impedance seal with said one or more cells of said cell culture.”

As set forth in the Hickman Declaration, the microelectrode of Jung et al. has gold microelectrodes with an insulating silicon nitride top layer. A silane self-assembled monolayer was formed on top of the insulator. The sensor of the prior art is asserted to produce a high resistance seal rather than a high impedance seal.

Note that claim 12 (dependent upon claim 1) specifically recites that the surface modifying agent of the intervening layer can be a self-assembling monolayer. Claim 13 specifically recites that the self-assembling monolayer can be silane. The specification indicates that such agents produce a high resistance rather than high impedance seal between the microelectrode and cell. (See for example specification page 56, section on alternative surfaces.) This is in contradiction to page 13, line 23, through page 14, line 12, which indicates that a self-assembling monolayer on the microelectrode provides a high impedance seal between microelectrode and cell. It is noted that a related application Hickman et al. (US 2003/0054333) discloses at paragraph [0044-0045] that a bare metal electrode coated with a SAM or biological macromolecule, in the absence of an insulating layer, creates a high impedance seal. The instant specification does not disclose that the high impedance seal requires no insulation and the instant claims do not preclude insulation. In fact, claim 7 is directed to an insulator being present.

Pages 44-45 of the specification indicate that moderate or high viscosity interface layers between the silane layer on the microelectrode and the cell can increase impedance. It does not speak to "high" impedance. No claim is directed to this particular microelectrode.

The specification does not appear to particularly disclose or provide guidance on how to produce the required high impedance seal. In addition, the specification and claims particularly contemplate including elements that would appear to result in a high resistance seal rather than a high impedance seal. See for example, page 17, of the instant specification which discloses an embodiment of the invention where the active surface of the microelectrode can comprise platinum black with an insulator just as in Jung et al.

Applicant is requested to point with particularity (page and line number) to any other parts of the specification that demonstrate or exemplify particular layers that produce the required high impedance seal such that one would know what microelectrode to build to result in the required properties.

Claim 7, 19, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is confusing in failing to clearly indicate where the insulator is positioned with respect to the microelectrode surface, intervening layer, and/or cells. As the intervening layer must be in contact with the microelectrode surface and this same layer must provide a high impedance seal with a cell, it appears that the insulator must be above or on top of the cell. Clarification is requested.

Claim 19 does not appear to further limit claim 18 in that all nucleic acid sequences encompassed by claim 18 would have known or unknown function. As such, claim 19 does not appear to differ in scope. Clarification is requested.

Claim 27 is confusing in reciting “deconvolution … provides information on pathways or functional categories affected in the cell.” It is not clear what the metes and bounds of functional category are nor what deconvolution analysis provides the recited information. The claim as written does not make clear what specific information must be provided to meet the limitation of the claims. Applicant does not appear to have responded to this ground of rejection.

***Claim Rejections - 35 USC § 103***

Claims 1-14, 18-19, 22-27, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borkholder et al. (U.S. Patent No. 6,377,057) in view of Hickman et al. (US 2003/0055333).

Applicant is being given benefit to the instant filing date of 5/22/00 and denied benefit to the priority date of 5/21/99 for provisional application 60/135,275. It is noted that the provisional application appears to be a compilation of two grant proposal documents and does not disclose or contemplate the generic invention as presently recited in the claims. Applicant has not pointed out by page and line number in the provisional document for the claimed system, particularly for a generic intervening layer in contact with the microelectrode surface which comprises a generic surface modifying agent and provides a high impedance seal with one or more cells.

Borkholder et al. discloses a biosensor for use in evaluating the effect of test compounds on ion channels in excitable cells. Borkholder et al. contemplates using cells which are genetically altered by exogenous and endogenous gene manipulation as well as stem cells that are able to differentiate into excitable cells. Computer software and systems for action potential analysis are disclosed. (See abstract; claims; figures; column 7, line 45, through column 8, line 13; column 11, line 5, through column 12, line 40; column 14, lines 14-35.) Although hippocampal cells (see claim 8) are not specifically mentioned at column 11, lines 5-25, these neuronal cells would have been routinely used by those in the art at the time of the invention for electrophysiological recording. (See for example, page 2, lines 17-19, and page 5, lines 26-28, of the specification in support of this assertion.) Borkholder et al. doesn't clearly disclose a

microelectrode as set forth in the claims; however, Borkholder et al. makes clear that any other suitable biosensor could be used in the disclosed system and method.

Hickman et al. (US 2003/0054333) discloses a biosensor with no insulating layer and a bare metal electrode coated with SAM or biological macromolecule to create a high impedance seal. (See at least paragraphs [0044]-[0045] and [0167].) Attractive and repulsive SAM surfaces are disclosed. (See at least paragraphs [0074]-[0078] and claims.) Use of hippocampal and cortical cells are disclosed. (See at least paragraphs [0097]-[0099].) Hickman et al. does not explicitly disclose a system with software comprising data processing instructions although the reference does disclose a method of using the biosensor for monitoring the signal and correlating the signal to the presence or absence of a bioaffecting substance. (See at least paragraphs [0046]-[0051].)

It would have been obvious to use the microelectrode of Hickman et al. in the system and method of Borkholder et al. One would have been motivated to do so as a matter of substituting another suitable and known biosensor.

### ***Conclusion***

No claim is allowed. It is noted that co-pending applications 09/880,138 and 09/928,708 (inventor Hickman in common) are directed to biosensors similar to those claimed in the instant claims. The co-pending claims are not directed to systems having devices and software. The co-pending claims do not appear to have limitations to high impedance seals at this time. Applicant is reminded to maintain a clear line of demarcation between applications to avoid double patenting rejections.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Klemic et al. (U.S. Patent No. 6,699,697) discloses planar patch clamp electrodes that form a high resistance seal between the electrode and cell membrane. (See column 2, lines 55-65, and claims.)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 571-272-0712. The examiner can normally be reached on Monday-Thursday, 5:30 am - 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*Marianne P. Allen*  
Marianne P. Allen  
Primary Examiner  
Art Unit 1631

5/24/04

mpa